CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

HN-TOLMAR, INC.-25HN057465

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE Years	3. SEX	4-6 REACTION ONSET		
		Day	Month	Year			Day	Month	Year
ACMM	HONDURAS	03	Feb	2016	9	Female	27	Feb	2025

7+13 DESCRIBE REACTION(S) (including relevant tests/lab data)

1) BROWN LIGHT BROWN DISCHARGE (Vaginal discharge (10046901), Vaginal discharge (10046901))
(05/Mar/2025 -) - Not Recovered/Not Resolved/Ongoing
2) HYPERTHERMIA (Hyperthermia (10020843), Hyperthermia (10020843))
Not Recovered/Not Resolved/Ongoing
3) HEADACHE (Headache (10019211), Headache (10019211))
(27/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing
4) COUGH (Cough (10011224), Cough (10011224))
Not Recovered/Not Resolved/Ongoing

Cont..

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ LIFE THREATENING
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- ☐ RESULTS IN PERSISTENCE OR SIGNIFICANT DISABILITY/INCAPACITY
- ☐ CONGENITAL ANOMALY
- ☐ OTHER MEDICALLY IMPORTANT CONDITION

II. SUSPECT DRUG(S)INFORMATION

14. SUSPECT DRUG(S)(include generic name)

1) Eligard® (Leuprolide acetate, Leuprolide acetate) (Suspect) (Injection)(Unknown)

Cont..

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☑ NA

15. DAILY DOSE(S)

1) (45 milligram(s), 1 in 6 Month)

16. ROUTE(S) OF ADMINISTRATION

1) Subcutaneous

21. DID EVENT REAPPEAR AFTER REINTRODUCTION ☐ YES ☐ NO ☑ NA

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) Precocious puberty [10058084 - Precocious puberty]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (20/Feb/2025 - Ongoing)	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

1)ACETAMINOPHEN(PARACETAMOL)

Cont..

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

1) PRECOCIOUS PUBERTY (10058084, Precocious puberty) (Continuing: Yes)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER

Name : Tolmar, Inc
701 Centre Avenue
Fort Collins, CO, 80526, UNITED STATES OF AMERICA
debbie.maierhofer@tolmar.comand+1-4129158447

Study Information
Study Name: NA
EudraCT Number:
Protocol No.: NA
Center No.:
Subject Id :

24.REPORT NULLIFIED ☐ YES ☐ NO

24b. MFR CONTROL NO.

HN-TOLMAR, INC.-25HN057465

24c. DATE RECEIVED BY MANUFACTURER

02/May/2025

24d. REPORT SOURCE ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL

DATE OF THIS REPORT

13/May/2025

25a. REPORT TYPE ☑ INITIAL ☐ FOLLOWUP

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

7+13 DESCRIBE REACTION(S) (including relevant tests/lab data) (Continuation...)

5) Pain in both breasts (Breast pain (10006298), Breast pain (10006298)(01/May/2025 -) - Not Recovered/Not Resolved/Ongoing)

6) Itching in both breasts (Pruritus breast (10050817), Pruritus (10037087)(01/May/2025 -) - Not Recovered/Not Resolved/Ongoing)

7) DIZZINESS (Dizziness (10013573), Dizziness (10013573)(27/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing)

8) NAUSEAS (Nausea (10028813), Nausea (10028813)(27/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing)

9) BONE PAIN (ESPECIALLY IN THE FEET) (Bone pain (10006002), Bone pain (10006002)(27/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing)

Event Description :

This Study report from HONDURAS was received by Adium via Patient Support Program (reference number: HN-ADIUM-HN-0098-20250306) on 06-MAR-2025 from a Consumer/Other Non-Health Prof regarding a Child 9 Years old Female patient who experienced "Hyperthermia, Brown light brown discharge, Cough, Headache, Dizziness, Nauseas and Bone pain" (Hyperthermia), (Vaginal discharge), (Cough), (Headache), (Dizziness), (Nausea), (especially in the feet) and (Bone pain) during Eligard (Leuprolide acetate) 45 milligram therapy for Precocious puberty. The needle component of the constituent device was not identified in the report. The report was sent to Tolmar on 07-MAR-2025.

The patient's medical history and current conditions included precocious puberty.

Concomitant medications included Acetaminophen.

On 20-FEB-2025, the patient began receiving Eligard 45 milligram, q 6 month via Subcutaneous use for precocious puberty (Lot number and Expiration date were not reported).

On an unspecified date (one week ago from date of this report), at an unknown time after the most recent dose of Eligard, the patient experienced unquantified hyperthermia, cough.

On 27-FEB-2025, 8 days after the most recent dose of Eligard, the patient experienced headache, dizziness, nauseas, bone pain (especially in the feet).

On 03-MAR-2025 (in source narrative reported as 05-MAR-2025 which is discrepant), 12 days after the most recent dose of Eligard, the patient experienced had a coppery red almost brown stain on her underwear, without pain, patient only observed that it was like a brown light secretion.

Corrective treatment was not reported.

Action taken with Eligard in response to the events was Dose Not Changed. De-challenge and re-challenge were Not applicable.

The outcome of Hyperthermia was Not Recovered/Not Resolved.

The outcome of Vaginal discharge was Not Recovered/Not Resolved.

The outcome of Cough was Not Recovered/Not Resolved.

The outcome of Headache was Not Recovered/Not Resolved.

The outcome of Dizziness was Not Recovered/Not Resolved.

The outcome of Nausea was Not Recovered/Not Resolved.

The outcome of Bone pain was Not Recovered/Not Resolved.

The reporter did not assess the seriousness or causality of the events in relationship to Eligard.

On 11-MAR-2025, a revised form was received by Adium via Asofarma a tu lado Patient Support Program (reference number: HN-ADIUM-HN-0098-20250306) from the information initially received on 06-MAR-2025 which updated the onset date for the event Vaginal discharge from 03-MAR-2025 to 05-MAR-2025.

On 05-MAR-2025, 14 days after the most recent dose of Eligard, the patient experienced a coppery red almost brown stain on her underwear, without pain, patient only observed that it was like a brown light secretion.

On 02-May-2025, follow-up information was received by Adium via the PSP Solutions (Patient Support Program) (“ASOFARMA A TU LADO) (reference number: HN-ADIUM-HN-0098-20250306) from a consumer (Patient's family member) (non-healthcare professional). New information included: Added two new non-serious events of 'Pain in both breasts' (Breast pain) and 'Itching in both breasts' (Pruritus) and a concomitant medication.

Concomitant medications included Vitamins.

Continuation Sheet for CIOMS report

On 01-May-2025, the girl had itching and pain in both breasts. No further information was available.

Corrective treatment was not reported.

Action taken with Eligard in response to the events was dose not changed. De-challenge and re-challenge were not applicable.

The outcome of Breast pain and Pruritus was not recovered.

The reporter did not assess the seriousness of Breast pain and Pruritus.

The reporter did not provide the causality of Breast pain and Pruritus in relationship to Eligard and Eligard unspecified device.

Listedness

Listedness of the events vaginal discharge, hyperthermia, headache, cough, dizziness, nausea, bone pain is retained as per previous assessment.

Breast pain>Eligard>Unlisted as per CCDS>07-Nov-2024
Breast pain>Eligard>Unlisted as per USPI>Feb-2025
Breast pain>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Breast pain>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Pruritus>Eligard>Unlisted as per CCDS>07-Nov-2024
Pruritus>Eligard>Unlisted as per USPI>Feb-2025
Pruritus>Eligard unspecified device>Unlisted as per USPI>Feb-2025
Pruritus>Eligard>Unlisted as per Canadian monograph>02-Apr-2025

Company Remarks (Sender's Comments) :

Evaluator comments (Tolmar): Causality
Vaginal discharge-Not related to drug and device,
Hyperthermia-Not related to drug and device,
Headache-Not related to drug and device,
Cough-Not related to drug and device,
Dizziness-related to drug and not related to device,
Nausea-related to drug and not related to device,
Bone pain -related to drug and not related to device,

FU-Breast pain ('Pain in both breasts') and Pruritus ('Itching in both breasts') event added. Tolmar assessed the event as non-serious since it does not meet the ICH seriousness criteria and is not an IME event. The reported events breast pain and Pruritus were assessed as related to drug with known safety profile of the drug and not related to device. Causality of the events vaginal discharge, hyperthermia, headache, cough, dizziness, nausea, bone pain is retained as per previous assessment.

14.SUSPECT DRUG(S) (Continuation...)

Product-Reaction Level

1) Drug	:	Eligard® (Leuprolide acetate)
Active Substance	:	1) Leuprolide acetate
Drug Characterization	:	Suspect
Form of Admin	:	1) Injection
Lot Number	:	1) Unknown
Daily Dose	:	(45 milligram(s), 1 in 6 Month)
Route of Admin	:	1) Subcutaneous
Indications	:	1) Precocious puberty [10058084 - Precocious puberty]
Therapy Dates	:	1) From : 20/Feb/2025 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) BROWN LIGHT BROWN DISCHARGE (Vaginal discharge - 10046901, Vaginal discharge - 10046901)

Causality as per reporter	:	Not Reported
Causality as per Mfr	:	Not Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable

2) HYPERTHERMIA (Hyperthermia - 10020843, Hyperthermia - 10020843)

Causality as per reporter	:	Not Reported

Continuation Sheet for CIOMS report

Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) HEADACHE (Headache - 10019211, Headache - 10019211)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) COUGH (Cough - 10011224, Cough - 10011224)
Causality as per reporter : Not Reported
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) Pain in both breasts (Breast pain - 10006298, Breast pain - 10006298)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) Itching in both breasts (Pruritus breast - 10050817, Pruritus - 10037087)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) DIZZINESS (Dizziness - 10013573, Dizziness - 10013573)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

8) NAUSEAS (Nausea - 10028813, Nausea - 10028813)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

9) BONE PAIN (ESPECIALLY IN THE FEET) (Bone pain - 10006002, Bone pain - 10006002)
Causality as per reporter : Not Reported
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) BROWN LIGHT BROWN DISCHARGE
CORE UnLabeled
2) HYPERTHERMIA
CORE UnLabeled
3) HEADACHE
CORE Labeled
4) COUGH
CORE Labeled
5) Pain in both breasts
CORE Labeled
6) Itching in both breasts
CORE Labeled
7) DIZZINESS
CORE Labeled
8) NAUSEAS
CORE Labeled
9) BONE PAIN (ESPECIALLY IN THE FEET)
CORE Labeled

2) Drug : Eligard® Unspecified Device (Leuprolide acetate)
Active Substance : 1) Leuprolide acetate
Drug Characterization : Suspect
Form of Admin : 1) Injection
Lot Number : 1) Unknown
Route of Admin : 1) Subcutaneous
Indications : 1) Precocious puberty [10058084 - Precocious puberty]

Continuation Sheet for CIOMS report

Action(s) Taken With Drug : Not applicable

Causality

1) BROWN LIGHT BROWN DISCHARGE (Vaginal discharge - 10046901, Vaginal discharge - 10046901)
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

2) HYPERTHERMIA (Hyperthermia - 10020843, Hyperthermia - 10020843)
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

3) HEADACHE (Headache - 10019211, Headache - 10019211)
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

4) COUGH (Cough - 10011224, Cough - 10011224)
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

5) Pain in both breasts (Breast pain - 10006298, Breast pain - 10006298)
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

6) Itching in both breasts (Pruritus breast - 10050817, Pruritus - 10037087)
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

7) DIZZINESS (Dizziness - 10013573, Dizziness - 10013573)
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

8) NAUSEAS (Nausea - 10028813, Nausea - 10028813)
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

9) BONE PAIN (ESPECIALLY IN THE FEET) (Bone pain - 10006002, Bone pain - 10006002)
- Causality as per reporter : Not Reported
- Causality as per Mfr : Not Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

Labeling :

1) BROWN LIGHT BROWN DISCHARGE
   CORE
2) HYPERTHERMIA
   CORE
3) HEADACHE
   CORE
4) COUGH
   CORE
5) Pain in both breasts
   CORE
6) Itching in both breasts
   CORE
7) DIZZINESS
   CORE
8) NAUSEAS
   CORE

Continuation Sheet for CIOMS report

9) BONE PAIN (ESPECIALLY IN THE FEET)
CORE

15. DAILY DOSE(S) (Continuation...)

Dosage Text :

Drug 1 :Eligard®

1) 45 milligram, q 6 month

22.CONCOMITANT DRUG(S) (Continuation...)

1). Drug	:	ACETAMINOPHEN
Active Substance	:	1) PARACETAMOL
Form Strength	:	
Indications	:	1) Drug use for unknown indication [10057097 - Drug use for unknown indication]

2). Drug	:	VITAMINS NOS
Active Substance	:	1) VITAMINS NOS
Form Strength	:	
Indications	:	1) Drug use for unknown indication [10057097 - Drug use for unknown indication]